REMARKS

Status of the Claims

Claims 1 and 15, 16 and 18-33 are in the application.

Claims 1 and 15, 16 and 18-33 have been rejected.

By way of this amendment, claims 1, 22, 23 and 32 have been amended.

Upon entry of this amendment, claims 1, 15, 16 and 18-33 will be pending.

Summary of the Amendment

Claims 1 and 23 have been amended to more clearly define the invention. as amended, the claims clearly recite that the amplified RNA product is not labeled. Support for the amendment is found throughout the claims as filed and the specification, such as on page 11, lines 28-29. No new matter has been added.

Claim 22 has been amended to correct an obvious typographical error.

Claim 32 has been amended to change its dependency to claim 23. Support for the amendment is found throughout the specification and claims as filed. No new matter has been added.

Objection

Claims 31 has been objected to as being substantially duplicative of claim 32.

Claim 32 has been amended to change its dependency from claim 1 to claim 23. Accordingly, the objection is moot. Applicants respectfully request that the objection be withdrawn.

Obviousness-type Double Patenting Rejections

Claims 1, 15, 16 and 18-33 have been rejected on the grounds of non-statutory, obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 7,045,286.

Applicants respectfully note that pending claims remain rejected on other grounds. Upon an indication of allowability of claims, Applicants shall promptly file a terminal disclaimer as appropriate.

Claims 1, 15, 16 and 18-33 have been provisionally rejected on the grounds of non-statutory, obviousness-type double patenting as being unpatentable over claims 1 2, 4 and 12 18 of co-pending application Serial No. 10/856,057.

Applicants respectfully note that this a provisional obviousness-type double patenting rejection because the conflicting claims have not yet been patented. If claims in co-pending application Serial No. 10/856,057 are indicated to be allowable and claims of the pending application are additionally indicated to be allowable, Applicants will promptly file a terminal disclaimer as appropriate. At this time, no terminal disclaimer is required.

Claims 1, 15-16 and 18-33 have been provisionally rejected on the grounds of non-statutory, obviousness-type double patenting as unpatentable over claims 1-4 of co-pending application Serial No. 10/333,542. Applicants respectfully note that this a provisional obviousness-type double patenting rejection because the conflicting claims have not yet been patented. If claims in co-pending application Serial No. 10/333,542 are indicated to be allowable and claims of the pending application are additionally indicated to be allowable, Applicants will promptly file a terminal disclaimer as appropriate. At this time, no terminal disclaimer is required.

Applicants invite the Examiner to contact Applicant's undersigned representative at (610) 640-7855 should the Examiner deem claims, which are rejected on the grounds of non-statutory, obviousness-type double patenting, otherwise allowable. Applicants shall promptly prepare and file by telefax terminal disclaimer as appropriate.

Rejection under 35 U.S.C. §103

Claims 1, 15, 16 and 18-33 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Eberwine et al. (U.S. Patent No. 5,922,553) in view of Fields et al. (WO 94/26932) and Waggoner (U.S. Patent No. 5,627,027).

Eberwine et al. discloses a method of immuno-aRNA using an RNA promoter on a cDNA sequence covalently coupled to an antibody which binds to a selected protein. Amplified RNA product is produced using radiolabeled nucleotides to produce a labeled amplified RNA product that has the radionucleotides incorporated within in by covalent bonds.

Waggoner discloses cyanine dye molecules that are specifically designed and intended to be used to covalently bond to molecules to be labeled such as fragments of DNA or RNA.

Fields et al. discloses a nucleic acid tagged immunoassay in which the oligonucleotide is attached to a ligand using a biotin streptavidin linker.

It is asserted that one skilled in the art at the time of the invention was made would have been motivated to modify the method of Eberwine et al. by applying fluorescent dye as taught by Waggoner to stain amplified RNA because Waggoner indicated cyanine dye is highly light absorbing. It is asserted that it would have been *prima facie* obvious to apply the cyanine dye for detecting and quantifying molecules expressing the selected epitope sample. It is asserted that one skilled in the art would have been motivated to apply the biotin streptavidin linker for attaching the oligonucleotide to the monoclonal antibody as taught by Fields et al. Applicants respectfully disagree.

Applicants respectfully assert that the combination of references does produce the claimed invention. Applicants respectfully assert that the combination of references does not teach or suggest the claimed invention. Applicants respectfully assert that the combination of references teaches away from the claimed invention. One skilled in the art, viewing the references, would not be motivated to produce the claimed invention but instead would be taught to practice different subject matter than the claimed invention. One skilled in the art, viewing the references, would be motivated to practice subject matter that is explicitly contrary to the claimed invention as taught in the specification.

Eberwine et al. discloses a method which is "semi-quantitative" (see Eberwine column 2, line 34). Eberwine does not disclose a quantitative method in which the detectable signal is directly proportional to molecules expressing the selected epitope in the sample. Eberwine does not disclose linking the cDNA sequence to the antibody by a non-covalent bond. Eberwine does not disclose unlabeled RNA amplification product. Eberwine does not disclose the use of fluorescent dye to stain the RNA amplification product.

Waggoner specifically discloses cyanine dyes which are used to label, i.e., covalently bond to molecules sought to be detected (See Waggoner, column 2, lines 1-5; column 2, lines 25-32; column 2, lines 56-61; column 4, lines 35-42; column 7, lines 47-52; column 7, lines 61-65; column 8, lines 50-59; and column 9, lines 20-27). The specific purpose and intention of Waggoner is that the fluorescent label is covalently linked to the molecule to be detected. The invention in Waggoner is to provide the means to affect such covalent linkage. Waggoner expresses teaches away from non-unlabeled detection. Waggoner specifically teaches away from non covalent use of the dyes. Waggoner does not disclose unlabeled RNA amplification product. The point of Waggoner is to provide labeled materials such as labeled RNA. Waggoner does not disclose the use of fluorescent dye to stain unlabeled RNA. Waggoner does not disclose a quantitative method in which the detectable signal is directly proportional to molecules expressing the selected epitope in the sample.

Fields et al. does not make up for these deficiencies found in both Eberwine and Waggoner. Fields et al. does not teach non covalent use of the dyes. Fields does not disclose unlabeled RNA amplification product. Fields et al. does not disclose the use of fluorescent dye to stain unlabeled RNA. Fields et al. does not disclose a quantitative method in which the detectable signal is directly proportional to molecules expressing the selected epitope in the sample.

The combination of Eberwine et al., Waggoner and Fields et al. does not produce a *prima facie* case of obviousness of the claimed invention. The combination does not yield the claimed invention. Moreover, Waggoner teaches away from the claimed invention.

Eberwine et al. specifically teaches covalent linkage radiolabeled nucleotides within the amplified RNA product. Those skilled in the art combining Eberwine et al., Waggoner and

Fields et al. would neither be motivated nor conclude to produce an unlabeled stained RNA amplification product. Nothing in the combination of Eberwine et al., Waggoner and Fields et al. teach or suggest non-covalently linked fluorescent staining of RNA amplification product. To the contrary, Waggoner specifically teaches away from non-covalent linkage. Moreover, nothing in the combination of Eberwine et al., Waggoner and Fields et al. teach or suggest a quantitative method in which the detectable fluorescent signal is used to stain unlabeled amplification product such that the detectable fluorescent signal is directly proportional to molecules expressing the selected epitope in the sample The combination of Eberwine et al., Waggoner and Fields et al., neither teach nor suggest the claimed invention.

The claimed invention is not obvious in view of combination of Eberwine et al., Fields et al. and Waggoner. Applicants respectfully request that the rejection of claims 1, 15-16 and 18-33 under 35 U.S.C. §103(a) as being unpatentable over Eberwine et al. in view of Fields et al. and Waggoner be withdrawn.

Conclusion

Claims 1, 15, 16 and 18-33 are in condition for allowance. A notice of allowance is earnestly solicited.

The Commissioner is hereby authorized to charge any deficiencies of fees and credit of any overpayments to Deposit Account No. 50-0436.

Respectfully submitted,

/Mark DeLuca, Reg.#33,229/
Mark DeLuca, Reg. No. 33,229

March 21, 2007

Pepper Hamilton LLP
400 Berwyn Park
899 Cassatt Road
Berwyn, PA 19312-1183
Telephone: 610.640.7855
Facsimile: 267.430.7635